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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,345	02/22/2002	Martin Karpf	20407 US1	2961

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER

KHARE, DEVESH

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/081,345

Applicant(s)

KARPF ET AL.

Examiner

Devesh Khare

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2. 6) ☐ Other: _____

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Minor objections

Claims 6,7 and 13 are objected to because of the following informalities:

Claims 6 and 7 are objected to for failing to end in a period.

Claim 13, line 3; misspell the word "methanesulfonate".

Appropriate correction is required.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kent et al. (U.S. Patent 6,204,398).

Claims 1 and 2 are drawn to a process for preparing a 2-aminoalcohol (III) by treating a 1,2-epoxide of formula (II) with an amine in the presence of a magnesium halide catalyst. Additional claim limitations include the amine of formula R^5NHR^6 wherein the amine is allylamine, diallylamine, benzylamine, dibenzylamine or trimethylsilyl amine and the magnesium halide catalyst is magnesium bromide diethyl etherate.

Claims 3 and 4 are drawn to a cyclohexene carboxylate derivative of the formula (X) and pharmaceutically acceptable addition salts. Claim 4 limits claim 3 in that the compound is (3R,4S,5R)-5-amino-3-(1-ethyl-propoxy)-4-hydroxy-cyclohex-1-ene carboxylic acid ethylester.

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Claims 5-7 are drawn to a cyclohexene carboxylate derivative of the formula (XI) and pharmaceutically acceptable addition salts. Claims 6 and 7 limits claim 5 in that the R^5 NHR^6 substituent at position 5 is allylamino or formylamino.

Claims 8-10 are drawn to a cyclohexene carboxylate derivative of the formula (XII) and pharmaceutically acceptable addition salts. Claims 9 and 10 limits claim 8 in that the R^5 NHR^6 substituent at position 5 is allylamino and the $R^4 R^3 N$ substituent at position 4 is acetylamino or amino.

Claims 11-13 are drawn to a cyclohexene carboxylate derivative of the formula (XIII) and pharmaceutically acceptable addition salts. Claims 12 and 13 limits claim 11 in that the R^5 NHR^6 substituent at position 5 is formylamino or amino and the $R^4 R^3 N$ substituent at position 4 is methanesulfonyl. Additionally, the compound of claim 13 is an addition salt of methanesulfonate (1:1).

Kent et al. teach the synthetic methods and compositions of cyclohexene carboxylate derivatives (see formulas (I)-(IV)). Kent et al. disclose a process for preparation of a 2-aminoalcohol (col. 20, lines 45-67 and col. 21, lines 1-25) by treating a 1,2-epoxide of formula (40) with an amine (eg. benzylamine: amine reagent of formula HY^1 , where Y^1 is defined as substituted amino group, see col. 20 lines 61-65) in the presence of a base. Kent et al. does not suggest the use of magnesium halide catalyst in the reaction; however Kent et al. teach the use of a base with the amine reagent (col. 21, lines 21-22). Kent et al. disclose the preparation of 2-aminoalcohol enriched or resolved optical isomers at any or all asymmetric atoms (Col. 27, lines 60-65), however the Kent et al.

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patent is seen to render the instantly claimed process for preparing the non-chiral isomers of 2-aminoalcohol *prima facie* obvious.

Kent et al. disclose the cyclohexene carboxylate derivatives and their compositions (col. 1, lines 10-11), especially compound 50 (col. 21), compound 71 (col. 23), compound 11 (col. 2), which are closely analogous to the applicant's claimed compounds of claims 3-13; Kent et al's cyclohexene carboxylate compounds and compositions differ from applicant's cyclohexene carboxylate compounds and compositions in that the cyclohexene carboxylate derivatives, R^{11} and R^{12} are not defined as an alkyl group or substituted alkyl group.

Applicants claim, namely (3R,4S,5R)-5-amino-3-(1-ethyl-propoxy)-4-hydroxy-cyclohex-1-ene carboxylic acid ethylester(claim 4), the compounds where the $R^5 NHR^6$ substituent at position 5 is allylamino or formylamino (claims 6 and 7), the compounds where the $R^4 R^3 N$ substituent at position 4 is acetylamino or amino (claims 9 and 10) and the $R^5 NHR^6$ substituent at position 5 is formylamino or amino and the $R^4 R^3 N$ substituent at position 4 is methanesulfonyl (claims 12 and 13) and their compositions. Applicants use of "cyclohexene carboxylate" core structure in the claimed compounds is rendered obvious because Kent et al's disclose the compounds and compositions, which is seen to "comprise" the "cyclohexene carboxylate" core structure (see col.21 (50), col.23(71) and col.2(11)). It would have been obvious to modify the compounds of formula (II) and (IV) in abstract, of the Kent et al. patent by substituting the Markush groups on the "cyclohexene carboxylate" core structure. Use of a known member of a class of materials in a process is not patentable if other members of the class were known to be

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useful for that purpose, even though results are better than expected. Kent et al. provide motivation to use cyclohexene carboxylate derivatives as inhibitors of neuraminidase (col. 1, lines 35-44).

Therefore, one of ordinary skill in the art would have found the applicants process for preparing a 2-aminoalcohol and the compounds and compositions of cyclohexene carboxylate derivatives, to have been obvious at the time the invention was made having the above reference before him because Kent et al. teach the a process for preparation of 2-aminoalcohol and the cyclohexene carboxylate derivatives and their compositions. A skilled artisan would be motivated to make routine modifications to produce the cyclohexene carboxylate derivatives for pharmaceutical delivery.

State of the Art References

The following references further reflect the current state of the art:

Kent et al. (U.S. Pub. No. 2002/0058823) -discloses the preparation of cyclohexene carboxylate derivatives.

Kent et al. (U.S. Pub. No. 2002/0156300) -discloses the preparation of cyclohexene carboxylate derivatives.

Kent et al. (U.S. Patent 6,518,438) – discloses the preparation of cyclohexene carboxylate derivatives.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is (703)605-1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Devesh Khare, Ph.D., JD(3Y).

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March 13, 2003



SAMUEL BARTS
PRIMARY EXAMINER
GROUP 1800